

Application No. 10/522,690

REMARKS

In response to the restriction requirement, claims 1-25 are pending and subject to a restriction requirement mailed September 19, 2007 (the Restriction Requirement).

Herein, Group I having claims 1-12, 21, 22, and 25 is elected with traverse as explained below. Claims 1 and 19 are amended to recite a liquid middle phase, e.g., as at page 21, first paragraph of the specification. Claims 13, 14, 16-18, and 23-24 are amended to remove element numbers.

The Restriction Requirement placed the claims into three Groups: Group I having claims 1-12, 21, 22, and 25 for a method for crystallization of macromolecules in a three-phase system; Group II having claims 13-18 and 23-24 drawn to a device for crystallization of macromolecules in a three-phase system; and Group III having claims 19 and 20, drawn to a three-phase system for crystallization of macromolecules.

The Restriction Requirement found no unity of invention based on a lack of same/similar special technical features. This position was based on an argument that Mayer et al. (JMB, 1999, 292:871-891) taught the limitations of claim 1. Referring to the Restriction Requirement Figure at page 3, the "upper phase" would be the oil layer, the "middle phase" would be the air/N<sub>2</sub>, and the "lower phase" would be the precipitant, with the "fourth phase" being the protein.

Firstly, amended claim 1 is directed to a lower aqueous phase, a middle liquid phase and an upper hydrophobic phase. Claims 19 and 20 already specified three liquid phases. Mayer et al. does not disclose, among other things, a middle liquid phase. Therefore Mayer et al. does not teach the claimed special technical feature and withdrawal of the restriction is requested.

Secondly, claim 1 is directed to, among other things, the case wherein "said middle phase is selected to have a diffusion of water from the fourth phase into the lower phase". The problem with the Restriction Requirement's argument is that the alleged gaseous middle phase of Mayer et al. (as suggested in the Restriction Requirement Figure at page 3) does not separate the fourth protein phase of Mayer et al. from the lower phase because the gaseous phase, even in the Figure, is not placed between the lower phase and the fourth phase. Accordingly, the middle-gaseous-phase is not selected to have a diffusion of water from the protein-fourth-phase into the precipitant-protein

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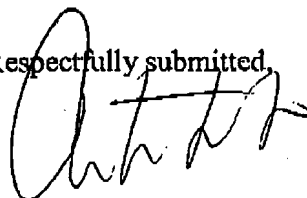
lower-phase. The gaseous-middle-phase does not involve such diffusion. Therefore Mayer et al. does not teach the claimed special technical feature and withdrawal of the restriction is requested.

Moreover, Mayer et al. teach away from a fourth phase because they use a solution having a final concentration of "3.3 mg/ml after equilibration", i.e., after thorough mixing with the precipitant/Tris buffer, see page 886, right column, last paragraph. Therefore, the person skilled in the art gets no incentive to develop a separate phase, as in the claimed three-phase/four-phase system.

Indeed, one advantage of the present invention relates to providing a method for obtaining crystals of macromolecules as homogenous and large as possible (page 5, first paragraph of the specification). This advantage is addressed by the three-phase/four-phase system as claimed, wherein the lower phase is an actual distinct phase and does not even mix with the fourth phase until the crystallization begins in the fourth phase or at a phase boundary (claim 1). Therefore a person skilled in these arts would not arrive at the claimed method for crystallization of macromolecules.

The Examiner is invited to telephone the undersigned if the Examiner believes it would be useful to advance prosecution.

Respectfully submitted,



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